

CONCEPT

DETAILED PARAMETERS

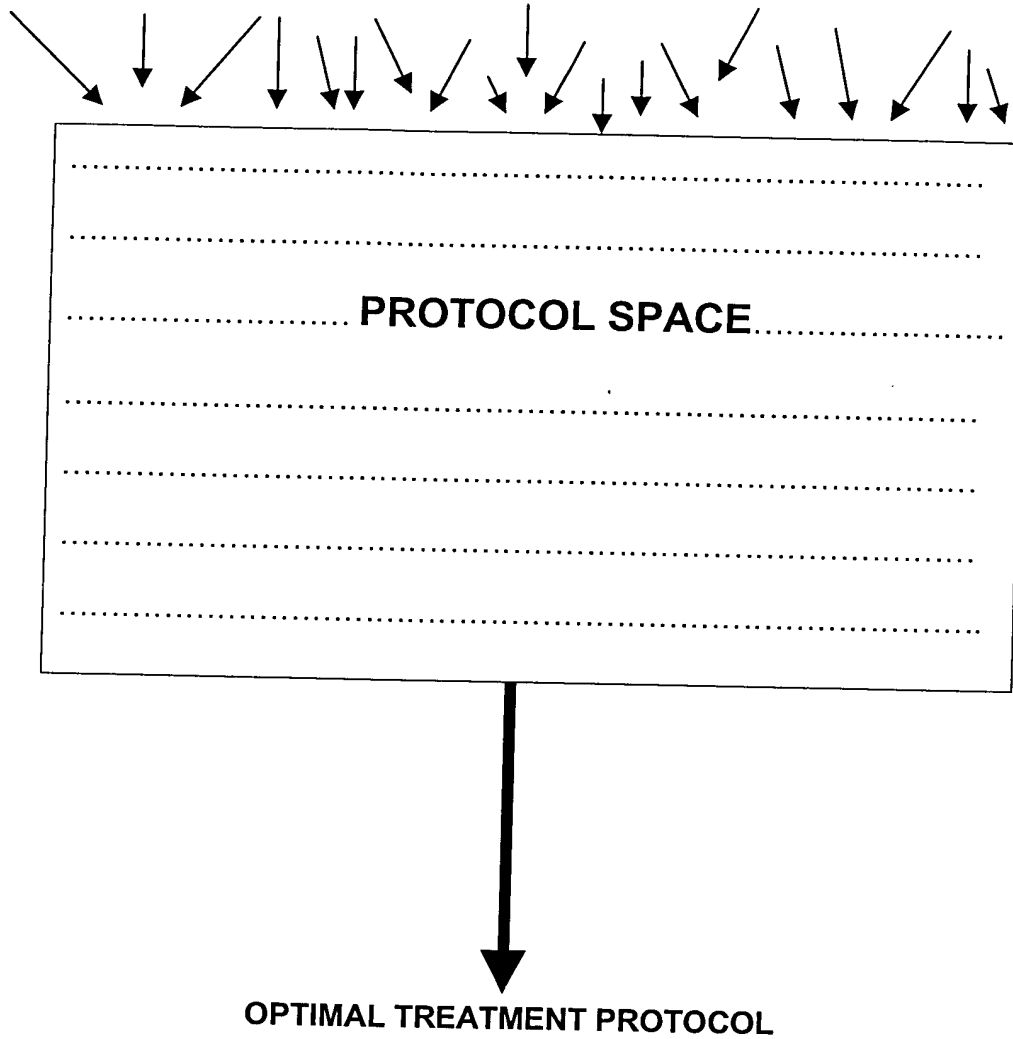


Fig. 1

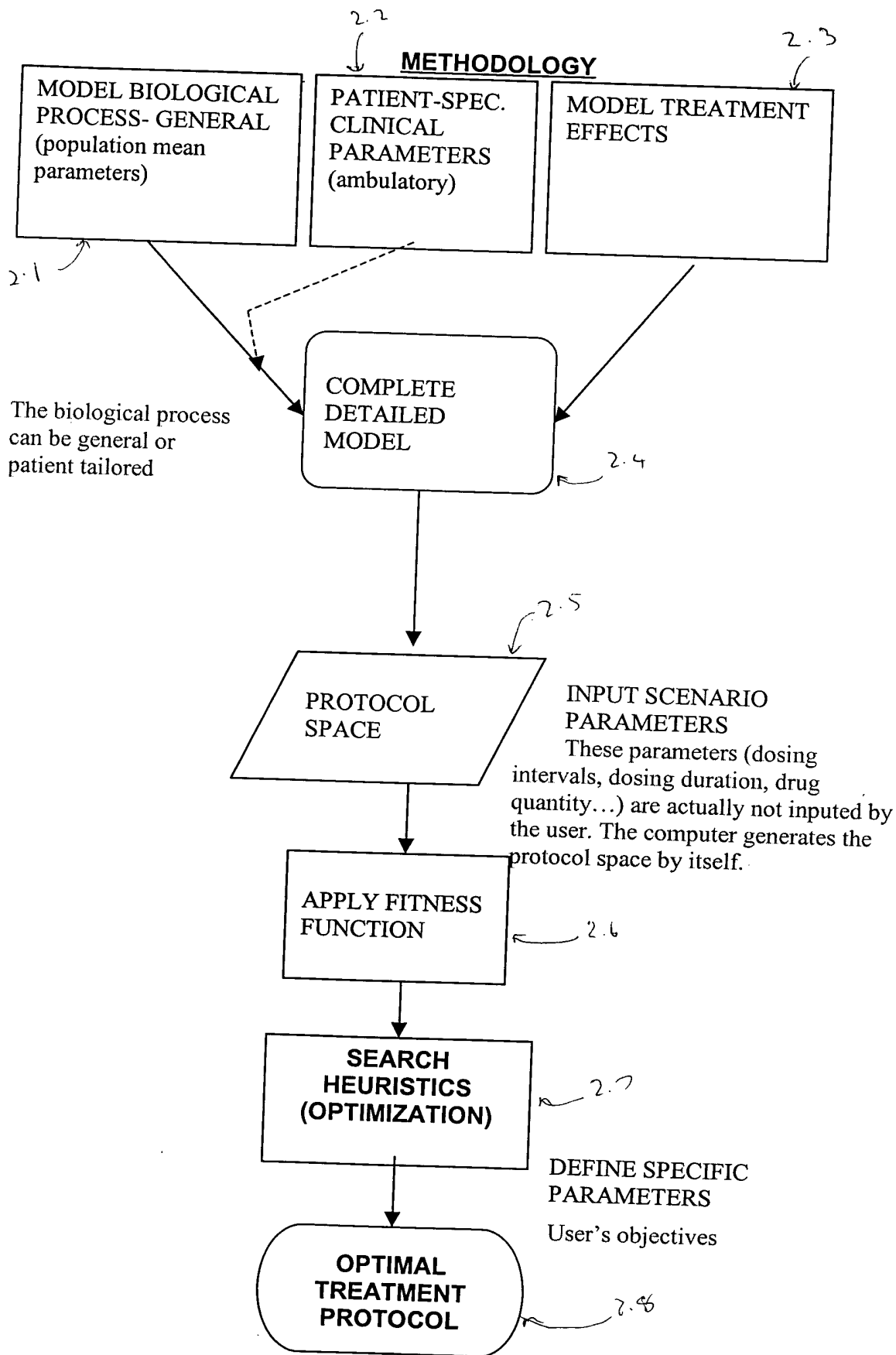


Fig. 2

METHODOLOGY (2)

Attempting to optimize some instance of
a chemotherapy problem with a given
set of solutions...

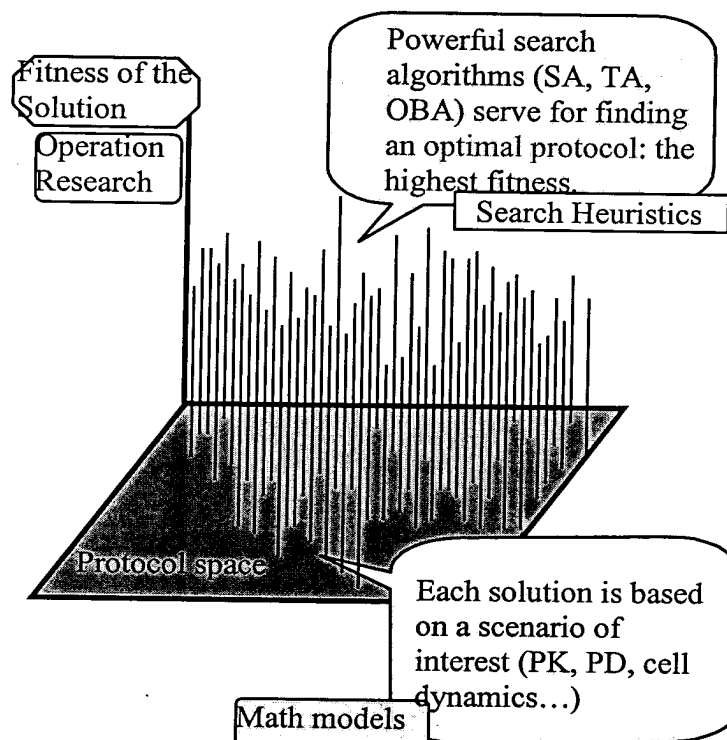


Fig. 2a

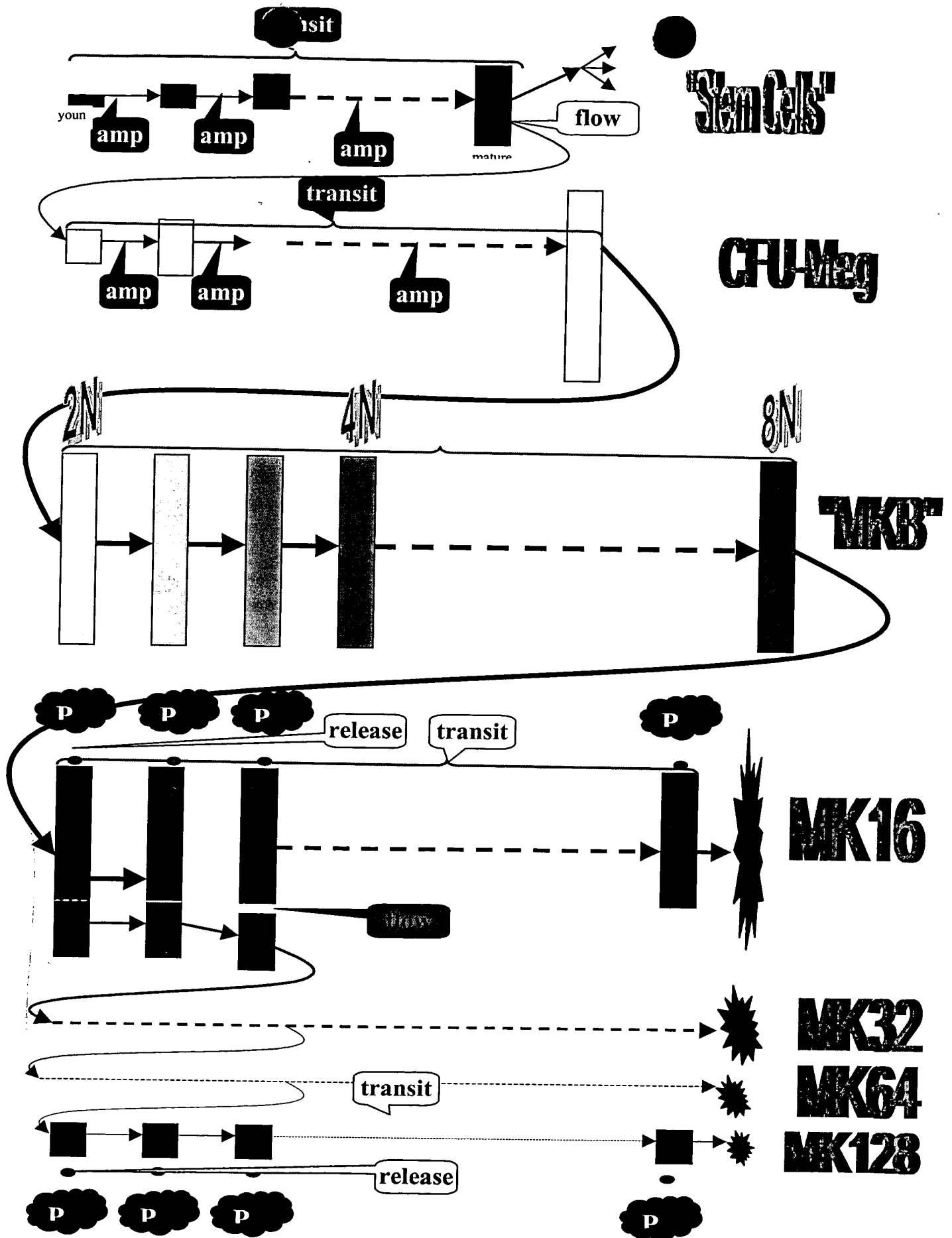


Fig. 3

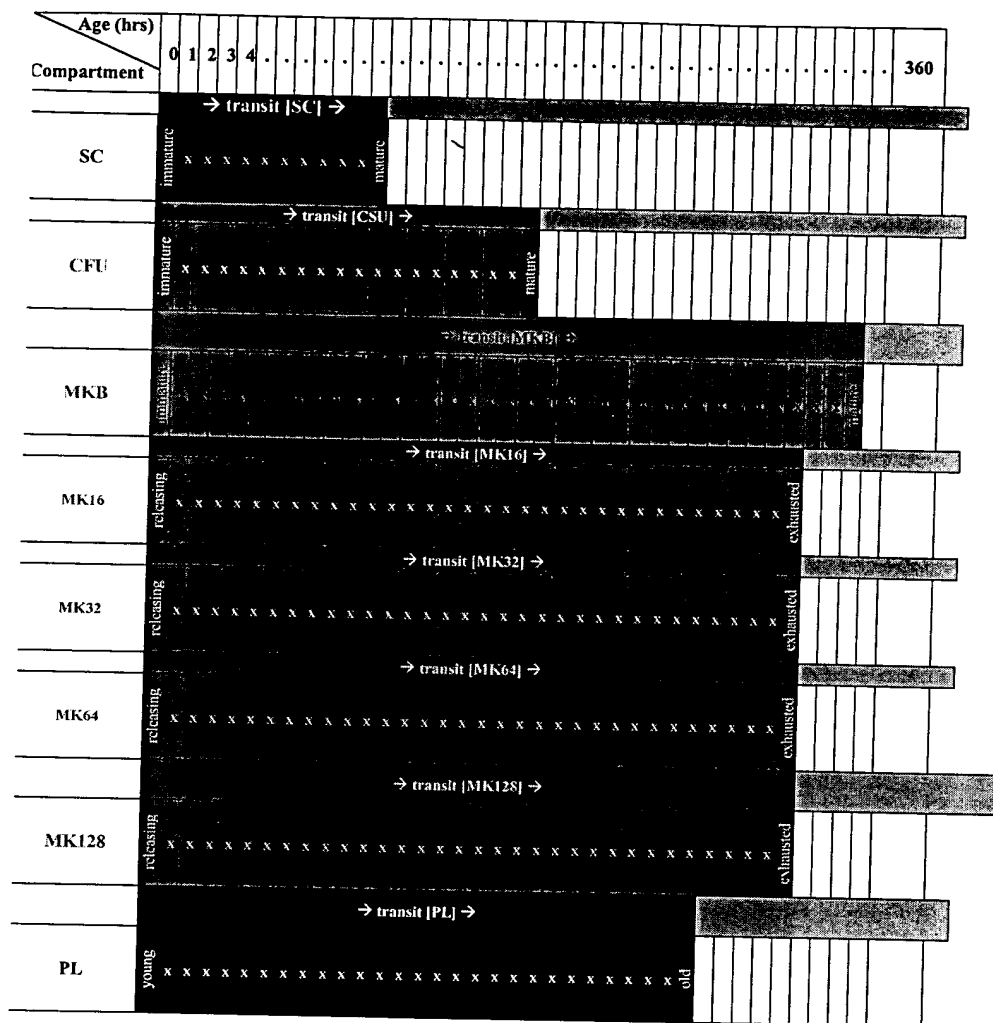


Fig 4

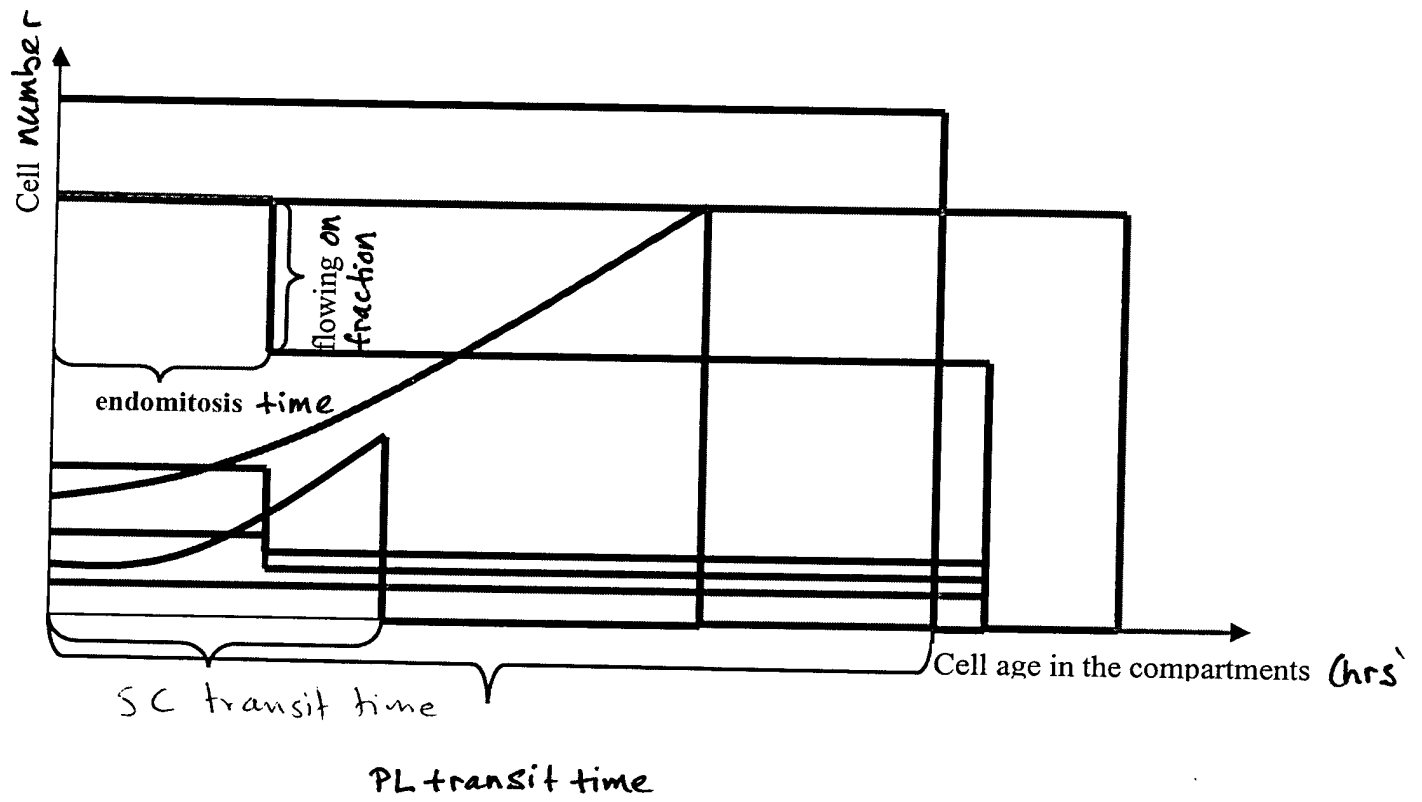


Fig. 5

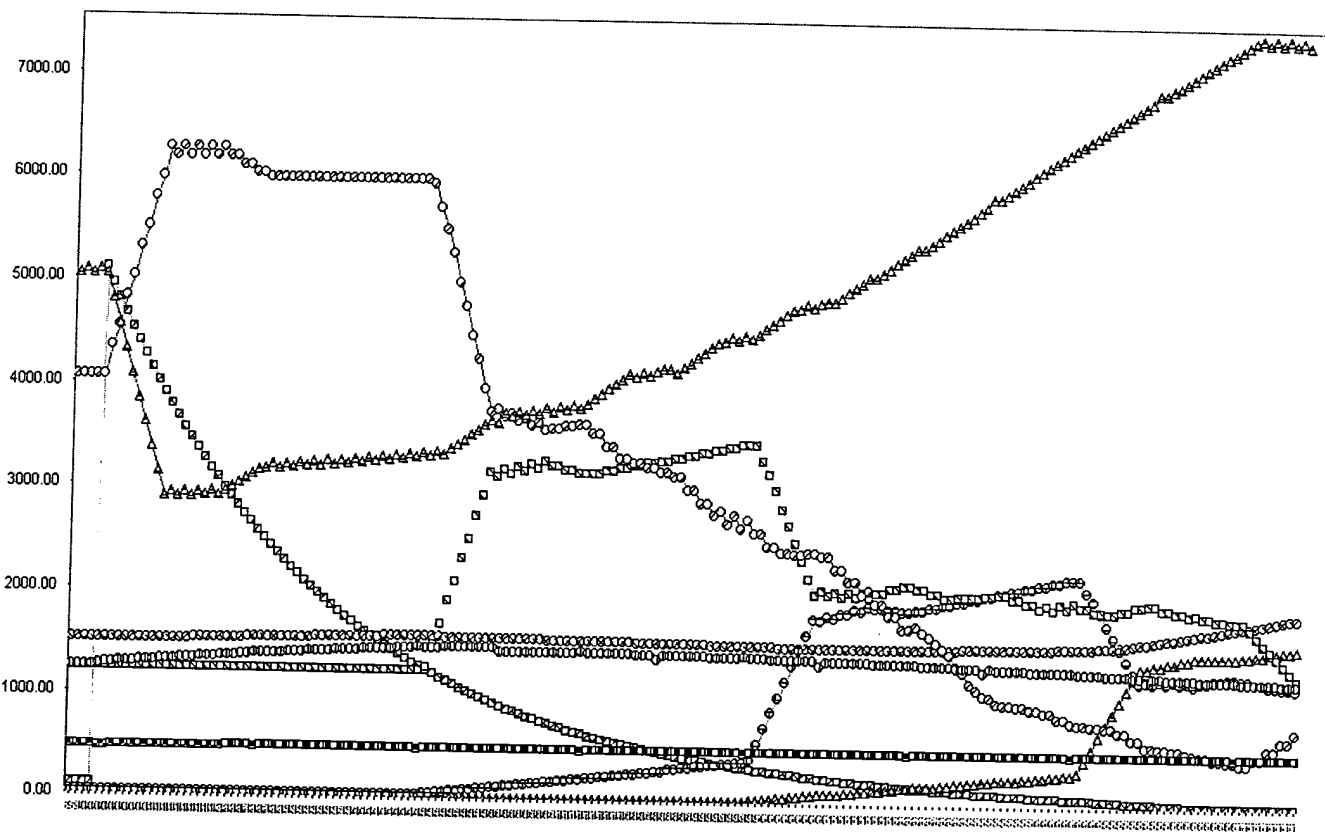


Fig. 7

Simulations showing that if the protocol is pre-calculated then a similar or a higher efficacy can be obtained using 4-fold reduced total dose of TPO.

TPO use in healthy donors:

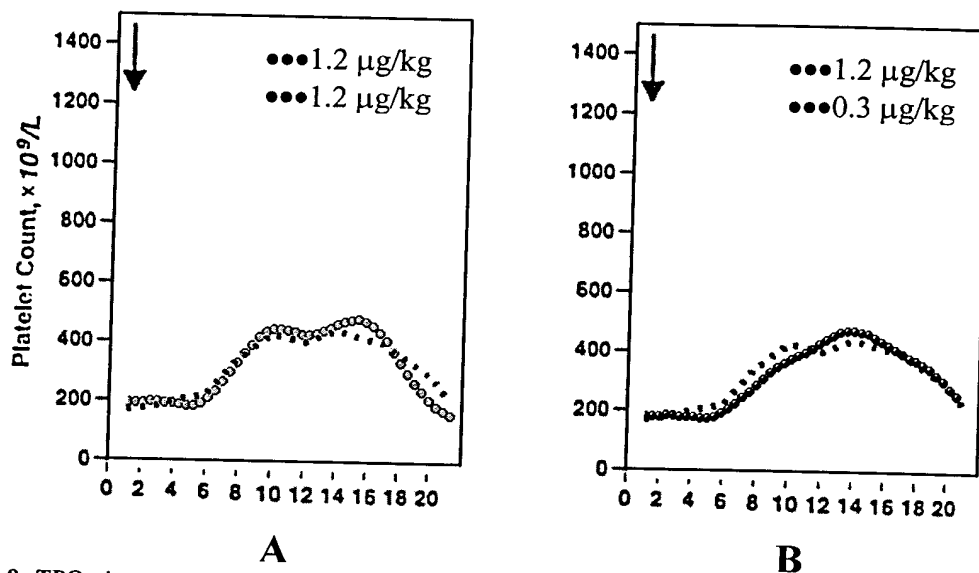


Fig. 8: TPO given to healthy donors- Results of TPO clinical trials from recent research on healthy platelet donors, as compared to our computer simulation results. Arrows indicate the start of TPO treatment. (A) Comparison of experimental data from published articles¹ (black) and our model simulation (green), in both TPO was given as a single IV dose of 1.2 µg/kg on day 0. (B) Comparison of the same experimental data (black) and our proposed TPO administration protocol; the total dose in the simulated protocol was 0.3 µg/kg (blue).

TPO use in patients receiving chemotherapy:

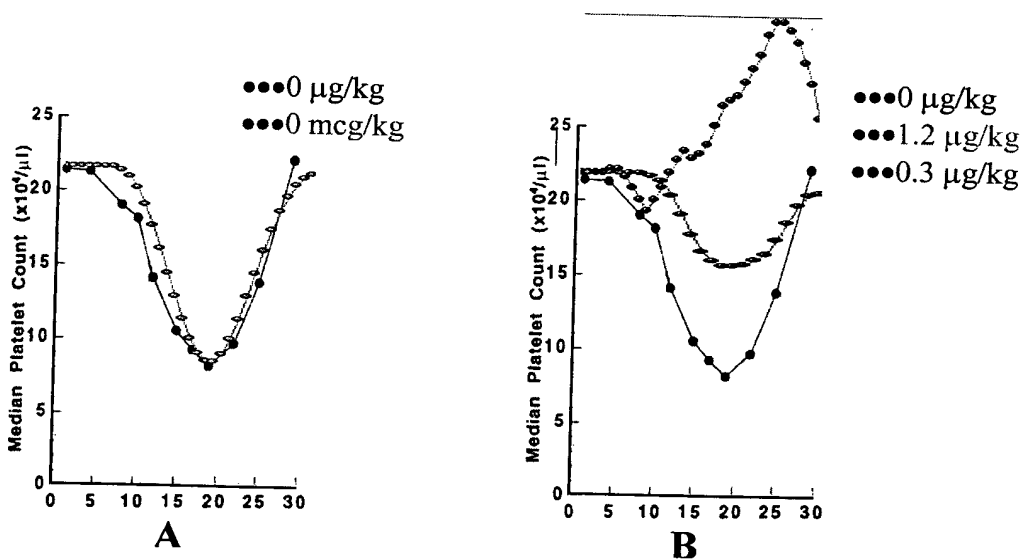


Fig. 9: TPO with chemotherapy- (A) Results of clinical trials from recent research on thrombocytopenia induced in patients receiving single carboplatin chemotherapy² on day 0 (black), as compared to our model simulation of these results (green). (B) The same experimental data (black); simulations of the same experiment, with addition of "conventional" TPO protocol of a single IV dose of 1.2 µg/kg on day 0 (olive); simulations of the same experiment under our proposed protocol that totals 0.3 µg/kg (blue).

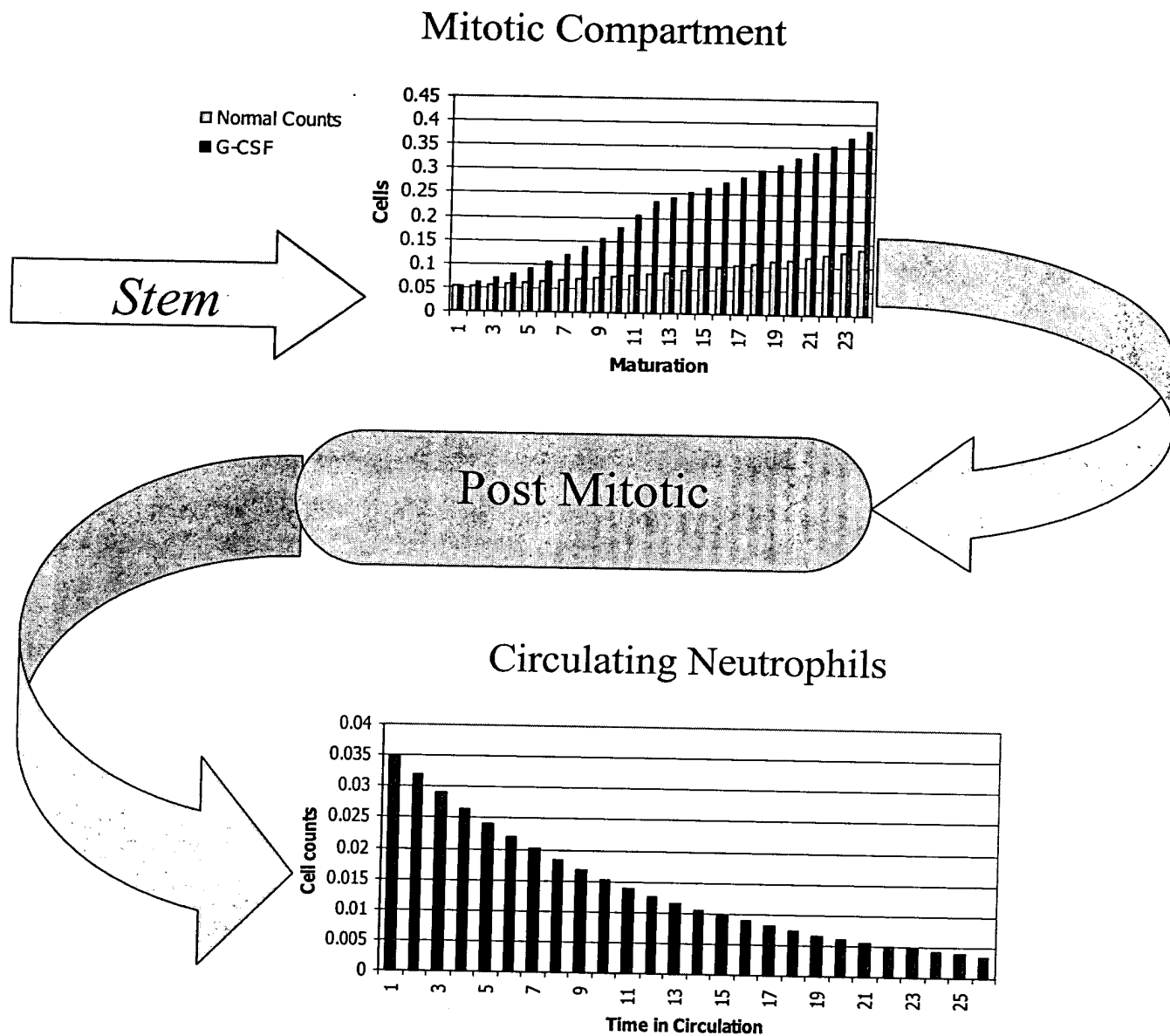


Fig. 10

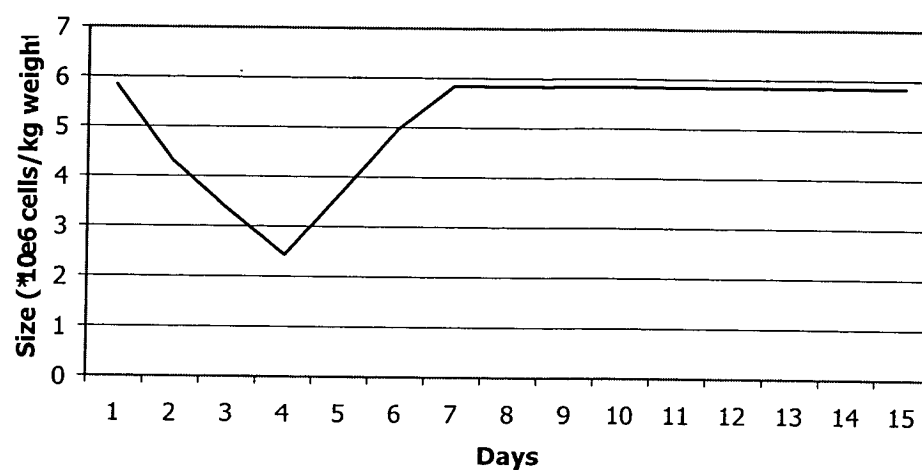


Fig. 11

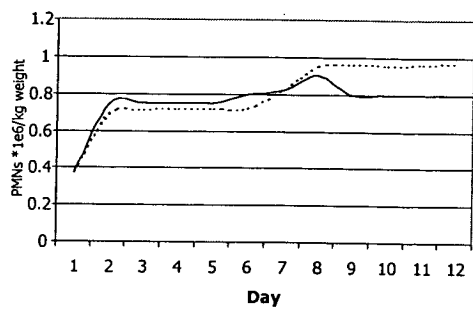


Fig. 12a

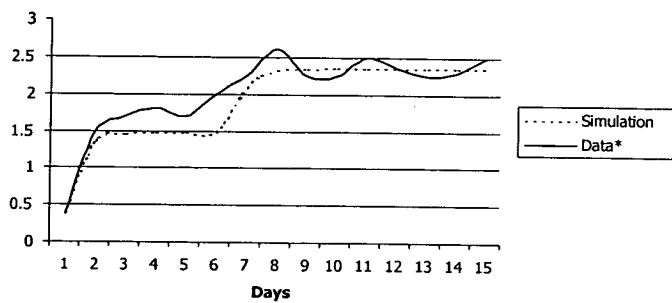
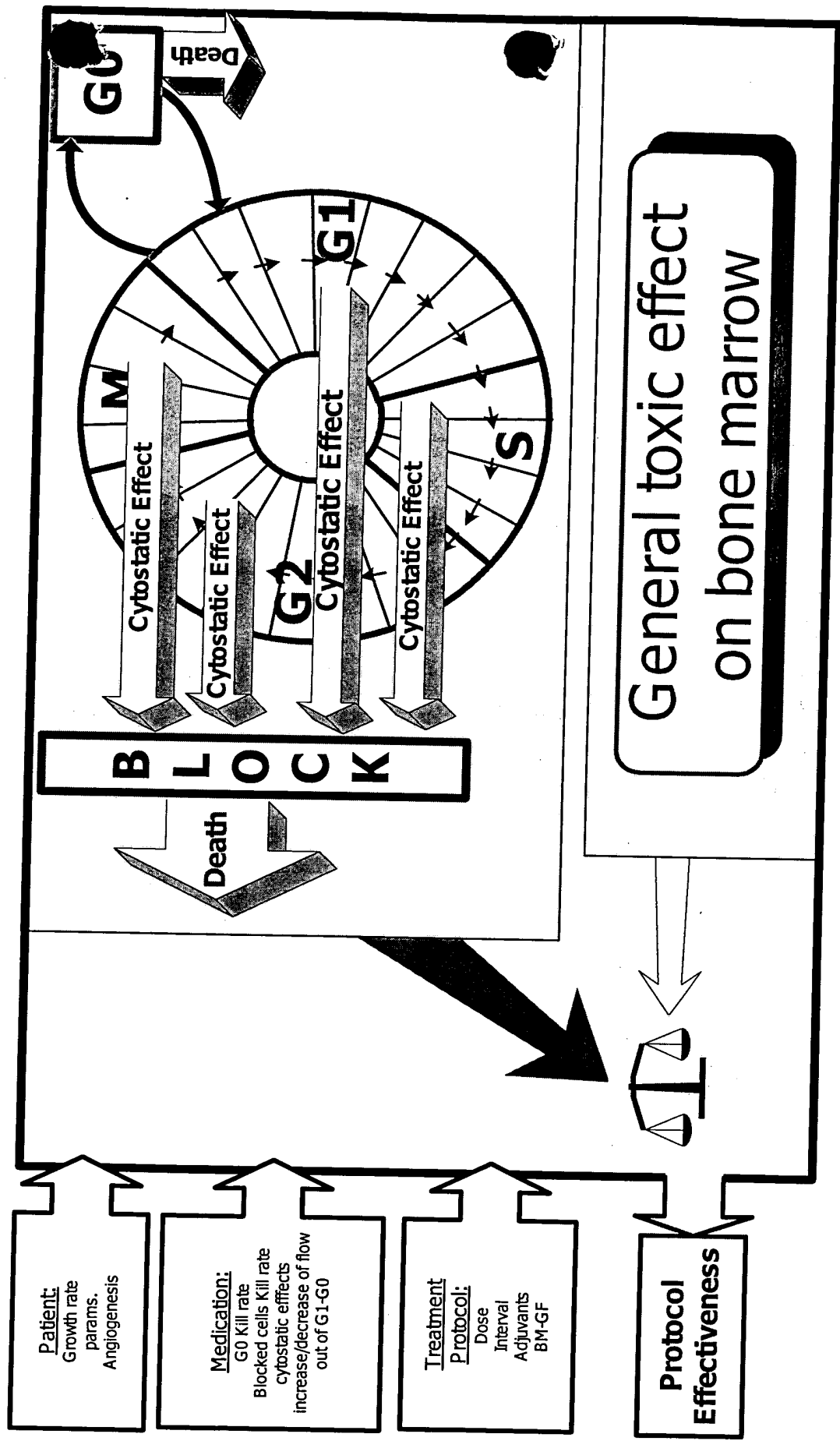


Fig. 12b

Diagram illustrating the effects of a treatment protocol on the cell cycle and bone marrow toxicity.



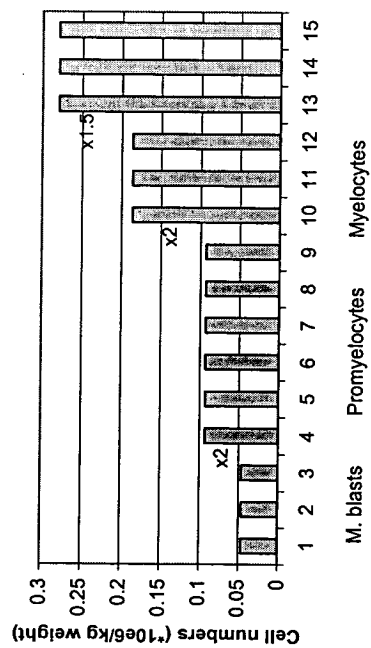


Fig 14. Simulated mitotic compartment age distribution and amplification values in untreated humans. Each bar represents a grouping of 8 cohorts of one hour. Amplification is noted at the place of occurrence.

Bar chart showing the relative number of myelocytes and promyelocytes in the peripheral blood of patients with acute myeloid leukaemia (AML) at different stages of disease. The Y-axis represents the relative number (0 to 1.2) and the X-axis represents the stages (1 to 15). The chart is divided into two sections: 'M. blasts' (stages 1-6) and 'Promyelocytes' (stages 7-15). The bars show a general increase in the relative number of myelocytes and promyelocytes as the disease progresses, with a significant peak at stage 15.

Stage	Relative Number (approx.)	Category
1	0.05	M. blasts
2	0.05	M. blasts
3	0.05	M. blasts
4	0.05	M. blasts
5	0.05	M. blasts
6	0.05	M. blasts
7	0.15	Promyelocytes
8	0.25	Promyelocytes
9	0.35	Promyelocytes
10	0.45	Promyelocytes
11	0.55	Promyelocytes
12	0.65	Promyelocytes
13	0.85	Promyelocytes
14	1.05	Promyelocytes
15	1.15	Promyelocytes

Metamyelocytes undergoes mitosis, but its effects are dampened in this graph due to the 8h grouping.